An Estimate of the Proportion of Symptoms Reported in Self-Administered Questionnaires That Are Captured as Adverse Drug Events in an Observational Database

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Purpose: This study was conducted to determine how frequently self-reported symptoms are captured as adverse drug events (ADEs) during chart abstraction. **Method:** We studied Ontario Cohort Study (OCS) participants attending the Toronto Hospital Immunodeficiency Clinic and compared OCS data on ADEs collected semi-annually through chart review and a self-administered questionnaire, completed on up to three occasions, which asked about the frequency, severity, and chronicity of symptoms including diarrhea, nausea, fatigue, and changes in body shape. Among 64 participants who completed the questionnaires, the median age was 42 years, the median time since HIV diagnosis was 9 years, 84% were male, 58% were men who had sex with men, 70% had viral load levels below 50 copies/mL, and the median CD4 was 422 cells/mm^3. All patients were taking antiretroviral therapy. **Results:** The median (interquartile range) number of symptoms per participant reported on the questionnaire at the first visit was 3 (1–5). The most common symptoms reported by patients were diarrhea (58%), headache (59%), difficulty sleeping (52%), dry skin (53%), and changes in body shape (52%). The median number of ADEs during the study period per participant in OCS was 1 (0–2). Of 345 symptoms identified on the questionnaire, 16% were reported as ADEs in the OCS. **Conclusion:** Although some symptoms were correctly not classified as ADEs as they were not related to antiretroviral medication, others may have been missed due to incomplete reporting to the physician, incomplete physician recording, or errors in chart extraction. **Key words:** *adverse drug events, chart extraction, questionnaire data*

Among people with HIV infection, antiretroviral-related adverse drug events (ADEs), such as gastrointestinal side effects, lipodystrophy, lipid abnormalities, and cardiovascular outcomes, are increasingly concerning. Cohort studies indicate that 36% to 50% of people living with HIV experience one or more adverse drug events (ADEs) attributable to antiretroviral therapy and up to 10% to 16% of these reactions are serious or severe.[1–4] An even larger percentage of patients experience symptoms, if we consider both symptoms that are a result of antiretroviral therapy and those due to HIV and its complications.[5] Symptoms are an important area of study because of the associated discomfort and because such symptoms may result not only in reduced adherence to medications and concern for drug resistance or treatment failure but also permanent discontinuation of drugs that can limit therapeutic options. Recent data suggest that symptoms occurring after initiation of ART are the most common reason that individuals discontinue HAART in the first year of treatment.[2,6] Symptoms

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can also result in significant costs associated with additional physician visits,[7] further medication to alleviate the symptoms, and tests to determine the etiology of the symptom as well as costs related to HIV complications that could result from interruption or discontinuation of ART.

Although randomized trials are the gold standard for estimating treatment effects, they are often not powered to estimate rates of ADEs that occur rarely, only after a significant exposure to the treatment, or only in subgroups of patients. For such ADEs, observational studies of large populations over prolonged periods may present superior research designs.[8] Two strategies for obtaining observational data on ADEs are chart reviews and self-administered questionnaires. Extraction of symptom data from charts may be inconsistent and incomplete due to failure of the patient to convey appropriate information to the clinician, failure of the clinician to adequately document the severity and frequency of the adverse event and its relationship to medication,[9] or failure of the chart abstractor to correctly interpret the medical record.[10] Even though self-administered questionnaires may be a good tool for measuring symptom burden, they are costly and less reliable for recording ADEs because patients may be uncertain as to whether or not the symptom is a result of the antiretroviral therapy. The design of self-administered questionnaires must strike a careful balance between enough questions to describe the symptoms in sufficient detail and too many questions that might overtax participants.

This study was conducted to determine how much of the symptom burden as reported on a self-administered questionnaire was captured by extracting data on ADEs from patient charts.

METHOD

We used two data sources for our study. The first, the Ontario Cohort Study (OCS), is a voluntary cohort study of more than 3,400 HIV-infected individuals receiving health care in Ontario, Canada, that records a broad range of information including clinical events, medication use, and laboratory results. The second data source was a self-administered questionnaire filled out by patients attending the Toronto Hospital Immunodeficiency Clinic. All patients attending the clinic from October 2002 to July 2004 who were OCS enrollees were invited to participate in the study. Ethics approval was obtained from the University Health Network, of which Toronto General Hospital is a member.

Ontario Cohort Study

The OCS recruits participants from HIV specialty and primary care clinics throughout the province of Ontario. More than 3,400 individuals have enrolled in OCS since 1994 and have ongoing data collection. As of December 2005, there were 660 OCS participants from the Toronto Hospital Immunodeficiency Clinic site, of which 296 were currently active patients. OCS participants complete a self-administered questionnaire at enrollment pertaining to demographic data and HIV testing and exposure history. All participants consented to have trained data extractors review their medical charts and extract detailed clinical, laboratory, and medication information. Information is recorded about adverse events believed to be related to medication for their HIV disease. ADEs are recorded using an open (spontaneous) model in which neither individuals nor data collectors are restricted in the type of ADE they may report, however, symptoms not specifically noted to be related to study medication are not recorded as adverse events. The OCS study is administered by the Ontario HIV Treatment Network, an independently incorporated, not-for-profit organization funded by the AIDS Bureau, Ontario Ministry of Health and Long-Term Care. OCS received research ethics approval from the University of Toronto as well as from the ethics boards of several hospitals where patients were enrolled.

Of the 991 active patients in the Toronto Hospital Immunodeficiency Clinic, 296 are OCS enrollees. Compared to the general clinic population at the Toronto Hospital Immunodeficiency Clinic, those who are enrolled in OCS are more likely to be male, men having sex with men (MSM), older, currently receiving protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), and less likely to have immigrated to Canada in the past 5 years.

Questionnaire

The self-administered questionnaire asked about fever, fatigue, headache, nausea, vomiting, diarrhea, rash, difficulty sleeping, mood changes, con-

fusion, kidney stones, numbness of hands or feet, dry skin or lips or ingrown toenails, and changes in body shape within the past 3 months. This list was composed of symptoms attributable to antiretroviral therapy but not tailored to the specific patient regimen. The WHO-ART,[11] ACTG,[12] and HIV Swiss Cohort[2] adverse event lists were used as models in developing our questionnaire. For each symptom, participants were asked about the severity, frequency, and chronicity of the symptom but not the likelihood that a symptom was a result of medication taken. Chronicity of a symptom was classified as *not within the past 3 months*, *ongoing problems* with the symptom, or *only within the past 3 months*. Frequency of the symptom within the previous 3 months was classified as *infrequent* (<7 days), a *few days* (7–13 days), *often* (14–40 days), and *frequent* (>40 days). Classification of the severity of symptoms varied according to symptoms and was based on the AIDS Clinical Trials Group (ACTG) classification. We intended to survey participants on three occasions (baseline, 3 months, and 6 months), but the number and timing of surveys varied somewhat. Patients completed the questionnaire before their visit with their physician.

ADE, demographic, and medication data were extracted from the OCS database for individuals who had completed at least one questionnaire. The frequency and types of symptoms reported on the questionnaires were compared to the ADE data extracted from OCS.

Statistical Methods

Demographic and clinical characteristics were summarized with numbers and proportions for categorical variables and medians and interquartile ranges for continuous variables. The numbers and proportions of patients experiencing a symptom at each visit and at any of the three visits were tabulated. The proportions of symptoms that were captured as ADEs in the OCS were tabulated by type of symptom, severity of symptom, frequency of symptom, and chronicity of symptom. The Cochran-Armitage test for trend was used to examine relationships between ordered categorical variables and the probability of a symptom being captured as an adverse event.[13] Adverse events with an onset date after the date of the last questionnaire or with a resolution date more than 90 days before the first questionnaire were excluded. Because the date of resolution of an ADE was not available for approximately two thirds of ADEs recorded in OCS, it was difficult to determine whether those ADEs occurred during the 3 months prior to administration of the questionnaire. Thus, ADEs from OCS with onset dates before the last questionnaire and with missing resolution dates were assumed to be ongoing during the study period. This strategy is likely to result in an overestimate of the proportion of symptoms that were recorded in OCS as adverse events.

RESULTS

A total of 64 participants filled out the questionnaire: 33 on three occasions, 21 on two occasions, and 10 on one occasion. The median numbers of months between the first and second visit and between the second and third visits were 5.5 (interquartile range [IQR] 3.2–9.0) and 4.9 (IQR 3.4–8.4), respectively. Of the 31 patients who completed fewer than three questionnaires, 6 were lost to follow-up and 25 continued to be followed in the clinic but declined to participate further in the study.

The majority of participants were male (84%), with a median age of 42 years (**Table 1**). The major self-identified risk factors for HIV infection were MSM (58%) and heterosexual sex (42%). Participants were generally healthy, with 70% having a viral load less than or equal to 50 copies/mL at the first visit and a median CD4 count of 423 cells/mm^3. At the first visit, 95% of the participants were taking nucleoside reverse transcriptase inhibitors (NRTIs), 64% were taking PIs, and 45% were taking NNRTIs.

The median number of symptoms reported at the first, second, and third visits were 3 (IQR 1–5, range 0–13), 3.5 (IQR 1–7, range 0–11), and 4.0 (IQR 2–7, range 0–11). The median number of symptoms per visit of patients who completed one or two questionnaires was 3 (IQR 1–5), compared to a median of 4 (IQR 2–8) among patients who completed three questionnaires (p = .15), indicating that patients who completed more visits had similar numbers of symptoms. In general, individuals were consistent in the level of reporting of symptoms across visits. Nine individuals (14%) did not report any symptoms during the study period, 9 individuals (14%) reported one or two symptoms, 20 individuals (31%) reported three to

Table 1. Characteristics of study population at first visit ($N = 64$)

Characteristic	
Age, years; median (IQR)	42 (37–47)
Gender, male; *n* (%)	54 (84%)
Risk factor for acquiring HIV[a], *n* (%)	
Men who have sex with men	37 (58%)
Injection drug user	2 (3%)
Heterosexual transmission	27 (42%)
Other	1 (2%)
Years since diagnosis, median (IQR)[b]	9 (3–13)
Viral load less than 50 copies/mL	45 (70%)
CD4 count cells/mm^3, median (IQR)	423 (254–636)
Medication use at first visit[c]	
Nucleoside reverse transcriptase inhibitor	61/64 (95%)
Non-nucleoside reverse transcriptase inhibitor	29/64 (45%)
Protease inhibitor	41/64 (64%)

Note: IQR = interquartile range.
[a]Individuals may have more than one risk factor.
[b]Years since diagnosis to first visit.
[c]Individuals may be taking more than one class of medications.

five symptoms, and 26 individuals (41%) reported six or more symptoms during the study period. Reporting of individual symptoms was less consistent, with mild events often starting or resolving and other events changing in frequency or severity. Eighty-five percent of patients reported at least one symptom at each of the three visits. The percentage of patients who reported at least one symptom that had appeared in the last 3 months varied between 30% and 46% at the three visits. The median numbers of ongoing symptoms and recent onset symptoms, per person per visit, were 2 (IQR 0– 5) and 0 (IQR 0–1), respectively.

Symptoms were summarized over visits by recording the worst severity, chronicity, frequency, and presence reported during the three visits for each patient (**Table 2**). The most common symptoms were diarrhea (58%), headache (59%), difficulty sleeping (52%), dry skin (53%), and changes in body shape (52%). The majority of events were ongoing. Among patients reporting a symptom, the symptoms most commonly described as severe were changes in body shape (21%), fatigue (19%), numbness in hands and feet (18%), and difficulty sleeping (18%). Among patients reporting a symptom, the symptoms most commonly described as occurring frequently (40+ days in past 3 months) were dry skin (41%), nausea (30%), difficulty sleeping (29%), diarrhea (28%), and numbness of hands and feet (27%).

Of the 225 adverse events reported in OCS at any time period for these patients, 98 (48%) of the records noted adverse events, comorbidities, or abnormal laboratory results that were not asked about in the questionnaire; 10 were duplicate events; and 30 ADEs were resolved at least 90 days before the date of the first questionnaire or commenced after the date the last questionnaire was completed. A total of 87 adverse events remained in the comparative analysis between the questionnaires and the OCS database. The OCS database did not capture any information about severity or frequency of the adverse events, and the duration of the event was inconsistently recorded.

Of 345 symptoms that were reported in the questionnaire, 57 (16%) were captured as adverse events in the OCS (**Table 3**). The symptoms most likely to be captured in the OCS were diarrhea (38%), nausea (35%), and changes in body shape (27%). The symptoms least likely to be recorded in OCS as ADEs were confusion (0%) and dry skin (0%). The frequency of a symptom was not associated with an increased likelihood that the event was recorded in OCS as an ADE (chi-square test for trend, $p = .34$). Severe symptoms were only slightly more likely than moderate or mild symptoms to be reported in OCS (21% vs. 19% and 15%) (**Table 3**). Of the 47 severe symptoms reported in the questionnaires, only 10 were recorded in OCS as ADEs. The 37 severe symptoms that were not recorded in OCS were lipodystrophy (6), headache (6), difficulty sleeping (4), fatigue (5), numbness in hands or feet (5), dry skin (3), nausea (2), vomiting (2), diarrhea (2), rash (1), and fever (1). A retrospective chart review of the 37 symptoms not recorded in OCS revealed that 10 (27%) were not mentioned in the chart at all, 5 (14%) were in the chart but not in OCS and presumably thought to be drug related, and 22 (59%) were in the chart but no indication of being drug related and thus were not adverse drug events.

Table 2. Presence, chronicity, severity, and frequency of adverse events as reported in questionnaire

Adverse event	Present	*n* (%)	Chronicity[a]	*n*[b] (%)	Severity	*n*[b] (%)	Frequency	*n*[b] (%)
Change in body shape	Yes	33 (52)	Ongoing	27 (82)	**LOSS** (face, arms, legs, buttocks)	4 (28)		
					Mild (noticeable only to self)			
			Recent onset	6 (18)	Moderate (noticeable to others – friends)	18 (64)		
					Severe (noticeable to strangers)	6 (21)		
					GAIN (abdominal, shoulders)	10 (50)		
					Mild (noticeable only to self)			
					Moderate (noticeable to others – friends)	6 (30)		
					Severe (noticeable to strangers)	4 (20)		
	No	30 (48)						
Confusion	Yes	18 (29)	Ongoing	14 (78)	Mild (lasted a short time)	9 (50)	Infrequently[c]	8 (44)
			Recent onset	4 (22)	Moderate (lasted longer but did not interfere with daily activities)	9 (50)	A few days	4 (22)
					Severe (interfered with daily activities)	0	Often	4 (22)
							Frequently	2 (11)
	No	45 (71)						
Diarrhea	Yes	37 (58)	Ongoing	29 (78)	Mild (3–4 loose stools per day)	25 (71)	Infrequently	7 (19)
			Recent onset	8 (22)	Moderate (5–7 loose stools per day)	5 (14)	A few days	8 (22)
					Severe (more than 7 loose stools/day)	5 (14)	Often	11 (31)
							Frequently	10 (28)
	No	27 (42)						
Fatigue	Yes	27 (42)	Ongoing	24 (89)	Reduced some activities	13 (50)	Infrequently	4 (15)
			Recent onset	3 (11)	Reduced many activities	8 (31)	A few days	9 (35)
					Reduced most of activities	5 (19)	Often	8 (31)
							Frequently	5 (19)
	No	37 (58)						
Fever	Yes	18 (29)	Ongoing	7 (39)	Mild (100–101.5°F)	9 (56)	Infrequently	10 (63)
			Recent onset	11 (61)	Moderate (101.6–102.9°F)	6 (38)	A few days	2 (12)
					Severe (103+°F)	1 (6)	Often	2 (12)
							Frequently	2 (12)
	No	45 (71)						

continued

Table 2. Continued

Adverse event	Present	*n* (%)	Chronicity[a]	*n*[b] (%)	Severity	*n*[b] (%)	Frequency	*n*[b] (%)
Numbness hand/feet	Yes	28 (44)	Ongoing	23 (82)	Mild (not interfering with function)	15 (54)	Infrequently	8 (31)
			Recent onset	5 (18)	Moderate (interfering with function but not daily activities)	8 (29)	A few days	5 (19)
					Severe (interfering with daily activities)	5 (18)	Often	6 (23)
							Frequently	7 (27)
	No	36 (56)						
Headache	Yes	38 (59)	Ongoing	26 (76)	Mild (no medication)	12 (32)	Infrequently	19 (53)
			Recent onset	8 (24)	Moderate (over the counter medication)	19 (51)	A few days	7 (19)
					Severe (prescription medication)	6 (16)	Often	9 (22)
							Frequently	2 (6)
	No	26 (41)						
Changes in mood	Yes	29 (46)	Ongoing	25 (86)	Mild (did not impact daily activities)	18 (62)	Infrequently	5 (17)
			Recent onset	4 (14)	Moderate (required therapy)	9 (31)	A few days	8 (28)
					Severe (severe anxiety or depression)	2 (7)	Often	13 (45)
							Frequently	3 (10)
	No	34 (54)						
Nausea	Yes	23 (36)	Ongoing	17 (74)	Mild (eating almost normally)	10 (43)	Infrequently	7 (30)
			Recent onset	5 (26)	Moderate (reduced food intake)	11 (48)	A few days	5 (22)
					Severe (very reduced food intake)	2 (9)	Often	4 (18)
							Frequently	7 (30)
	No	41 (64)						
Rash	Yes	11 (17)	Ongoing	6 (60)	Mild (redness/itchy skin)	7 (64)	Infrequently	1 (9)
			Recent onset	4 (40)	Moderate (causes significant discomfort)	3 (27)	A few days	2 (18)
					Severe (blistering, covers most of body)	1 (9)	Often	6 (55)
							Frequently	2 (18)
	No	53 (83)						
Dry skin	Yes	34 (53)	Ongoing	29 (91)	Mild (manages with moisturizers)	21 (61)	Infrequently	4 (13)
			Recent onset	3 (9)	Moderate (not managed with moisturizers or mild steroid cream)	10 (29)	A few days	7 (22)
					Severe (responds poorly to powerful steroid cream)	3 (9)	Often	8 (25)
							Frequently	13 (41)

continued

Table 2. Continued

Adverse event	Present	*n* (%)	Chronicity[a]	*n*[b] (%)	Severity	*n*[b] (%)	Frequency	*n*[b] (%)
Dry skin (continued)	No	30 (47)						
Difficulty sleeping	Yes	33 (52)	Ongoing	28 (85)	Mild (no medication)	10 (30)	Infrequently	5 (16)
			Recent onset	5 (15)	Moderate (minimal medication)	17 (52)	A few days	4 (13)
					Severe (not lessened by medication)	6 (18)	Often	13 (42)
							Frequently	9 (29)
	No	31 (48)						
Vomiting	Yes	14 (22)	Ongoing	8 (57)	Mild (2–3 episodes per day)	9 (75)	Infrequently	6 (43)
			Recent onset	6 (43)	Moderate (4–5 episodes per day)	1 (8)	A few days	6 (43)
					Severe (all foods and fluids)	2 (17)	Often	1 (7)
							Frequently	1 (7)
	No	50 (78)						
Kidney stones	Yes	3 (5)	Ongoing	3 (100)	Mild	1 (50)	Infrequently	2 (66)
					Moderate	1 (50)	A few days	0 (0)
					Severe	0 (0)	Often	1 (33)
							Frequently	0 (0)
	No	61 (95)						

[a]Recent onset means that the adverse drug event (ADE) appeared in the past 3 months.

[b]Numbers in subcategories may not always add up to the number of symptoms present due to missing data on chronicity, severity, and frequency.

[c]Infrequently (less than 7 days in past 3 months), a few days (7–15 days in past 3 months), often (14–40 days in past 3 months), frequently (40+ days in past 3 months).

Of the 87 ADEs reported in the OCS, 56 were reported on the questionnaires and 31 were not: rash (6), difficulty sleeping (5), mood (4), nausea (4), diarrhea (4), vomiting (3), numbness in hands and feet (2), headache (1), fatigue (1), and changes in body shape (1). Because the OCS data covered a wider time frame than the questionnaire, these symptoms may not have been bothersome to the patient at the time they completed the questionnaire.

DISCUSSION

We compared self-administered symptom questionnaires to ADE data extracted from charts. Our principal finding was that, among HIV-infected patients receiving antiretroviral therapy, only one in six self-reported symptoms was abstracted as an ADE. Although low, this proportion is likely an overestimate, because the time frame for chart extraction was wider than the reporting period for symptoms in the questionnaire.

Our findings should be interpreted with some caution, because we were comparing data collected for different purposes. The questionnaire asked patients to report their experience with a list of 14 symptoms, whether or not they were believed to be related to HIV medications; in contrast, chart abstraction only collected symptoms believed to have a relationship to current HIV medication. Furthermore, some symptoms have known relationships to therapy, such as lipodystrophy, while others may have multiple etiologies, such as difficulty sleeping. Nevertheless, even side effects that were

Table 3. Proportions of symptoms reported in questionnaire that are captured as adverse events in chart abstractions by type of event, severity, and frequency

Adverse event	*n* (%)
Type of event	
Changes in body shape	9/33 (27)
Confusion	0/18 (0)
Diarrhea	14/37 (38)
Fatigue	2/27 (7)
Fever	1/18 (5)
Numbness hand/feet	5/28 (18)
Headache	4/38 (11)
Changes in mood	1/29 (3)
Nausea	8/23 (35)
Rash	2/11 (18)
Dry skin	0/34 (0)
Difficulty sleeping	7/33 (21)
Vomiting	3/14 (21)
Kidney stones	1/3 (33)
Total	57/346 (16)
Severity	
Mild	25/172 (15)
Moderate	25/130 (19)
Severe	10/48 (21)
Unknown	1/9 (11)
Total	61/359 (17)
Frequency	
Infrequent	8/84 (9.5)
A few days	14/68 (21)
Often	11/85 (13)
Frequent	11/63 (17)
Unknown	3/11 (27)
Total	47/311 (15)
Chronicity	
Recent onset	8/66 (12)
Ongoing	38/236 (16)
Unknown	1/9 (11)
Total	47/311 (15)

Note: The numbers of events in the classification by severity are larger than the numbers of events classified by frequency or presence total because the changes in body shape were counted twice for classifications by severity, once for loss events, and once for gain events. "Frequency" was not recorded for "changes in body shape," thus the total number of events by frequency is less than the total number of events by type of event. All records for changes in body shape are removed for chronicity; the questionnaire did not distinguish between loss and gain events and whether they had separate onsets.

prevalent and commonly associated with antiretroviral medication, such as body changes, nausea, and diarrhea, were only recorded in one quarter to one third of OCS ADE records, suggesting that chart abstraction may miss many important patient-related outcomes.

Several explanations might account for missing ADE data in the OCS. Patients may tend to report a symptom in response to a prompt more readily than to volunteer it independently or to not have reported all symptoms to their physician due to forgetfulness, resolution of the symptom, or a desire to optimize the physician visit to deal with another issue. Physicians may also have incompletely recorded a symptom because it was previously documented, not thought to be important, or not thought to be drug related. Last, the chart abstractor may have overlooked some events in the data extraction process.

Although the frequency of incomplete recording varied from symptom to symptom, no symptoms were recorded in the chart as ADEs more often than reported on the questionnaire as symptoms. Some symptoms in particular, such as confusion, dry skin, and fever, were very poorly captured by OCS. A full four fifths of severe symptoms reported on questionnaires were not captured as ADEs in OCS. Almost two thirds of these severe symptoms were noted in the chart but not recorded in the database because they were not related to HIV medication, one quarter of the events were not recorded in the chart at all, and the remainder were not recorded in the database even though noted in the chart. Although some improvements in rates of reporting of symptoms can be achieved by improved chart abstraction procedures and more careful discussion of symptoms between patient and physician, the most important gain would be made through focusing on collecting data in the database on symptoms rather than ADEs if clinicians and researchers want to fully describe patients' experiences. Further, because the link between symptoms and drugs may not always be clear for unrecognized toxicities, focusing only on ADEs may underestimate the effects associated with newer medications.

Our results agree with those of other studies, which have also demonstrated poor agreement of patient and provider reports and underreporting of symptoms and of symptom severity by providers as compared to patients in both HIV-infected

individuals[14–16] and in other patient populations.[9,17] A 20-item self-completed HIV symptom index has been developed in an effort to standardize reporting and improve completeness of symptom documentation.[18]

Limitations of our study include the small sample size, the single site involved in the study, and the fact that we have not formally assessed the reliability or validity of our questionnaire. Despite this, we believe our findings demonstrate that databases dependent on chart abstraction of adverse events as a data collection tool are likely to significantly underreport patients' symptom burdens. We recommend implementation of symptom checklists in clinical settings to improve the quality of data for research purposes, but a full assessment of feasibility, including data quality, and cost remain outstanding.

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